IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	:	Dominic A. Cataldo, *et al.*
Serial No.	:	10/816,095
Filed:	:	April 1, 2004
For:	:	Use of Colloidal Clays for Sustained Release of Active Ingredients
TC/AU	:	1615
Examiner	:	Neil S. Levy
Attorney Docket No.	:	BGT 2-007

HONORABLE COMMISSIONER FOR PATENTS
MAIL STOP AF
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450

Sir:

Declarant, Dominic A. Cataldo, does declare and state that:

1. I have a B.S. degree from The Ohio State University, Columbus, OH, Major-Anatomy/Microbiology, 1966; M.S. from the University of Dayton, Dayton, OH, Major-Biochemistry/Physiology; and Ph.D. from Yale University, New Haven, CT, Major-Biochemistry/Physiology.
2. My work history is set forth on the summary CV, attached hereto and made a part hereof.
3. I am a co-inventor of and co-applicant in the above-identified application.
4. The current state of the art for sorbing solid compounds employs solution of the solid active ingredient so that the active ingredient molecules can be brought into intimate contact with the sorbent. If any solvent molecules are present in the treated nanoclays disclosed in the above-identified application, such solvent molecules would be adherent to the nanoclay as bound water of hydration or bound solvent of solvation. Hydrogen bonds are frequently involved. Thus, any water or other solvent involved in the above-identified application is not free; it is bound. These solvent molecules are distinguished from "free water" or "free solvent" of the art. The difference between bound solvent and free solvent is well known in drying technology. I refer the reader to the article on "Drying" in *The Encyclopedia of Chemical Technology,* 4th Edition, Volume 8, pp 475-519 (1993) and references cited therein. Conventional processes involve solution by dissolving the active ingredient in an appropriate solvent at a suitable temperature.

Success of the sorbent process then depends on the concentration of the active ingredient, the temperature of the solution, and the affinity of both the active ingredient and the solvent for sorption on sorbent sites. In other words, the solvent competes with the active ingredient for sorbent sites. The scientific bases for these processes are summarized in the article on "Adsorption" in *The Encyclopedia of Chemical Technology*, 4th Edition, Volume 1, pp 493-528 (1991) and references cited therein. The scope of the topic is confined to contact of fluid phases with solid sorbents. A person with ordinary skill in the art of adsorption would turn to this (or similar) sources to help understand the nanoclay process, but would not find useful information. The nanoclay materials of the above-identified application uses a mechanism not disclosed or recognized in these sources.

5. Usually, the sorption process includes attempts to remove the solvent by use of evaporation methods. These attempts may be more or less successful, because some of the solvent may be held tightly by the active ingredient molecules. Also, the sorbent may prefer the solvent over the active ingredient. The evaporation process may have a side effect in which the strongest sorbent sites are inhabited by the solvent, resulting in loosely held active ingredient molecules. This phenomenon would lead to more rapid active ingredient release rates. In addition, solvents frequently require expensive recovery and disposal systems. Many also raise health and safety issues. All in all, there is need for sorption systems that do not employ solvents.

6. Liquid active ingredients are frequently preferred over solids because they may permit use of less (or no) solvents. The solventless sorbent systems of the above-identified application avoid the problems cited above and, thus, render solid active ingredients more attractive. Furthermore, the absence of solvent residues in the end product can result in much longer product life.

7. The nanoclays of the above-identified application are especially useful in solventless sustained release systems. The nanoclay surface is covered with alkyl chains that are tethered to the clay particles by ammonium ion incorporation into the clay structure. The sorbent is a composite material that has organic chains that entangle the active ingredient. This sorption mechanism; thus, differs greatly from the traditional pore-based sorption mechanisms presented in the *Adsorption* article mentioned above. Information on nanoclay technology is available in numerous patents and at the web sites of the companies that manufacture these products. Especially useful are the following references: U.S. Patent No. 6,391,449, U.S. Patent No. 6,462,122, and "Barrier Enhancement" by Peter Maul, a paper available from Nanocor in Arlington Heights,

Illinois. These products are used to prevent permeation of gases into packaging materials. Nanocor scientists believe that the mechanism is formation of a torturous path for oxygen and carbon dioxide. Torturous path phenomena are part of the existing art (the article on "Barrier Polymers" in *The Encyclopedia of Chemical Technology*, 4th Edition, Volume 3, pp 931-962 (1992). The inventors of the above-identified application recognized the possibility that more than tortuosity may be involved. Entanglement effects, however, also could cause release of active ingredients to be less rapid.

8. These new processes would be rendered less successful when free water or other solvents are present. That is, when more than a few percent of solvent is present, organic solvents would interfere with the grappling action of the alkyl chains. Water would migrate to the hydrophilic portion of the active ingredient molecules and to the clay surface.

9. Based on the above differences between the new processes and traditional sorption processes, I am of the opinion that these sorbent processes to be both novel and useful in that no free solvents are present and the results show considerably greater sustained release properties

10. All statements made herein of our own knowledge are true and all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

FURTHER DECLARANT SAYETH NAUGHT.

D A Cataldo

Date: April 23, 2007

Dominic A. Cataldo